



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: ADDRESS FOR PATENTS AND TRADEMARKS
Washington, DC 20514
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09 761,466 | 01/16/2001 | Ike W. Lee | 01948-069002 | 5261 |

21559 75901 07/16/2002

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER

QIAN, CEJIN, X

ART UNIT

PAPER NUMBER

1636

DATE MAILED 07/16/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/761,466

Examiner

C Qian

Applicant(s)

LEE ET AL

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) 13-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 June 2001 is/are a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsman's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *Attachments*

DETAILED ACTION

Claims 1-17 are pending in the application.

Election/Restrictions

Applicant's election without traverse of Group I in Paper No. 11 is acknowledged.

Accordingly, claims 13-17 are withdrawn from consideration for being drawn to non-elected subject matter. Claims 1-12 are currently under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The nature of the invention is a nucleic acid comprising an cardiac specific enhancer element. The claims encompass 40-70 base pair nucleotides having 45%-100% homologies to a fragment of contiguous wild type nucleic acids (SEQ ID NO: 1-6). However, the specification only teaches that nucleic acids spanning A1+A2 region have cardiac enhancer activity. The specification does not teach which and what nucleotide within A1 or A2 is essential for the enhancer function. The specification fails to disclose a 50-70 base pair polynucleotide that having 45%-100% sequence homology with one of the SEQ IDs retains the enhancer activity. The prior art does not teach a nucleic acid having sequence homology as the claimed nucleic

acids that has enhancer activity. Therefore, the common structural feature or sequence by which the nucleic acids must share to function as a cardiac specific enhancer is unknown. As such, the invention was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The nature of the invention is a nucleic acid molecule comprising an enhancer element having sequence similarity to SEQ ID NO. 1-6 according to the limitation set forth in claim 1, 7, and 9-11. The claims are also drawn to a nucleic acid comprising 3 transcription factor binding sites selected from the group comprising Mef2, dHAND, GATA, TGF- β , CarG, E-box and Csx/Nkx2.5. The claims are further drawn to a vector comprising said nucleic acid. The specification discloses the isolation and characterization of a 5' fragment of human and mouse Csx/Nkx2.5 gene or sequence (see examples). The specification discloses that the consensus region between human and mouse sequence A1 and A2 have cardiac enhancer activity. However, said activity only exists when A1 + A2 are linked (see page 30, line 1).

The prior art does not teach an cardiac enhancer element located within 5' region of the Csx/Nkx2.5 gene, nor does the prior art teach any cardiac enhancer having sequence similarity as

SEQ ID NO: 1-6 as claimed. As such, one of skilled in the art would have to rely on the teaching of the specification to use the invention as claimed.

The breadth of the claims is broad and the teaching of the specification is limited. For example, claim 10 is drawn to a nucleic acid comprising a cardiac-specific enhancer element having at least 45% identity to 50 contiguous nucleotides of SEQ ID NO: 6. However, the specification teaches that SEQ ID NO: 6 is a consensus sequence between human and mouse that appears to have negative regulatory activity (see page 19, line 23 and Figure 2), whereas an enhancer increases basal transcription activity by a promoter alone. The specification fails to disclose the core functional elements or motifs that are required for the nucleic acid to function as a cardiac-specific enhancer. Nor does the specification teach which sequence the nucleic acid must have to transform the negative regulatory elements into positive elements. As such, it is unpredictable if a nucleic acid having at least 45% sequence identity to SEQ ID NO: 6 would function as a cardiac specific enhancer. By the same rationale, it is also unpredictable whether a nucleic acid having at least 100% identity to 50 contiguous nucleotides of SEQ ID NO: 6, at least 97% sequence identity to 60 contiguous nucleotides of SEQ ID NO: 6, at least 93% sequence identity to 70 contiguous nucleotides of SEQ ID NO: 6, or at least 90% sequence identity to 100 contiguous nucleotides of SEQ ID NO: 6 (claim 9) would function as a cardiac specific enhancer.

The specification also fails to teach a nucleic acid comprising either of the three transcription factor binding sites as recited in claim 8 functions as a cardiac enhancer. The specification only teaches a nucleic acid comprising A1 (SEQ ID NO: 1) and A2 (SEQ ID NO: 2) region increases transcription, wherein said region comprising the transcription factor binding sites as recited in claim 4 and 8). Without knowing which binding site is essential for the nucleic

acid to function as cardiac enhancer, it is unpredictable whether a nucleic acid comprising random combination of any of three elements claimed would function as a cardiac enhancer.

SEQ ID NO 3 and 4 comprise promoter region of Csx/Nkx2.5 that encompasses A1 and A2, that has cardiac specific enhancer activity. However, the specification fails to disclose the essential sequence elements that are required for enhancer function. Therefore, whether a 40 bp nucleic acid having 100% identity to SEQ ID NO:3, a 60 bp nucleic acid having 97% identity to SEQ ID NO 3, or a 70 bp nucleic acid having 95% identity to SEQ ID NO 3 (as claimed in claim 1) is unpredictable. By the same rational, whether nucleic acids sharing sequence homology to SEQ ID NO 4 would have enhancer function is also unpredictable. Since the specification discloses that A1 (SEQ ID NO 1) and A2 (SEQ ID NO:2) alone does not have enhancer activity, whether nucleic acids sharing sequence homology to these two fragments would have enhancer activity is also unpredictable.

In view of lack of teaching from the prior art and lack of guidance from the specification, one skilled in the art would have to engage in undue amount of experimentation to use the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1-12, the term "substantially purified" renders the claims indefinite because the degree of the purity of the nucleic acid is unknown. In other words, as defined by the specification, it is unclear how many and what genes the nucleic acid needs to be free from.

Regarding claims 7 and 10, the word "derive" renders the claims indefinite because the nature and the number of the derivative processes encompassed by the claims are unknown. As such, the metes and bounds of the claims cannot be established.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by McDonald et al (1995) and Lee (1995).

Claim 11 is drawn to a nucleic acid comprising 50 contiguous nucleotides that is at least 90% identical to 50 contiguous nucleotides of SEQ ID NO.4 or 5.

McDonald et al. disclose a polynucleotide comprising 80 contiguous nucleotides 100% identical to SEQ ID NO.5. Lee discloses a polynucleotide comprising 83 contiguous nucleotide 100% identical to SEQ ID NO.4. Therefore, McDonald et al. and Lee et al. disclose the instant claimed inventions. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
July 15, 2002



REMY YUCEL, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600